

# COMPUTATIONAL PREDICTION OF CONDENSED PHASE PROPERTIES FROM STATISTICAL CHARACTERIZATION OF MOLECULAR SURFACE ELECTROSTATIC POTENTIALS

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## Abstract

Macroscopic condensed phase properties that depend upon noncovalent interactions can be expressed analytically, to good accuracy, in terms of a small subset of a group of statistically-defined quantities that characterize molecular surface electrostatic potentials. The objectives are not only to develop predictive capabilities for the various properties, but as well to gain insight into the factors governing the interactions. The overall procedure is summarized conceptually in terms of a General Interaction Properties Function (GIPF). The statistical analysis of surface potentials also provides an effective basis for designing and evaluating molecules having specific types of interactive behavior. An overview of the general approach is presented, and a number of examples of various applications are discussed.

KEYWORDS: condensed phase properties, molecular surface electrostatic potentials, general interaction properties function (GIPF), solvation energies, heats of formation, diffusion constants

## Introduction

It has long been recognized that noncovalent interactions are predominantly electrostatic in nature [1-3]. This includes those due to dispersion forces, as was argued by Feynman [4] and confirmed by Hunt [5]. It would seem to follow that many physical properties that depend upon noncovalent molecular interactions – whether in crystals, liquids or solutions – should be quantitatively related to the features of the electrostatic potentials upon the molecular surfaces. As observed by Buckingham, “Both the electrostatic and induction energies are determined by the properties of the free molecules, so a knowledge of these properties is essential for a full understanding of intermolecular forces.” [6]. (As pointed out by Hirschfelder [2], induction forces are also electrostatic in nature.)

In a series of studies, which have been reviewed elsewhere [7-10], we have shown that a variety of condensed-phase macroscopic properties that reflect noncovalent interactions can be expressed analytically in terms of statistically-defined quantities that characterize molecular surface electrostatic potentials. These properties include heats of vaporization, sublimation and fusion, boiling points and critical constants, solubilities involving various solutes and solvents, free energies of solvation, Hildebrand solubility parameters, partition coefficients, surface tensions, diffusion constants, liquid viscosities, liquid and crystal densities, ionic lattice energies and impact sensitivities.

In the present paper, only a brief overview of these various applications will be given. Our focus shall be upon the conceptual basis of our approach, the details of the

methodology, and the physical insights that can be obtained from the results. We will also show how they can be combined with computed gas-phase energetics to yield other condensed-phase properties that are normally not readily accessible by theoretical methods.

## **Approach**

### *General*

Our basic concept is that properties depending upon noncovalent interactions can be represented quantitatively, with good accuracy, in terms of key features of molecular surface electrostatic potentials (plus the surface area, which is clearly an extensive variable that affects the strength of the interaction). This is an essential distinction between our approach and various structure-activity relationships that have been developed (for reviews, see [11-18]). They use descriptors that are intended to be measures of certain presumed elements of an interaction, e. g. hydrogen-bonding ability, polarizability, etc. In contrast, we have sought to identify quantities that will allow us to characterize most effectively the electrostatic potential over an entire molecular surface.

### *Molecular Surface*

Of course the first question must be how to define the surface, since it cannot be done rigorously. Various possibilities have been explored [19-26], a popular one being to use the outer surface of a set of intersecting spheres centered on the nuclei and having, for

example, the van der Waals radii of the respective atoms. However our preference has been to take the surface of a molecule to correspond to a particular contour of its electronic density  $\rho(\mathbf{r})$  [23-25], since this will reflect features such as lone pairs and strained bonds that are unique to that molecule. Following Bader *et al* [25], we choose  $\rho(\mathbf{r}) = 0.001$  au to be the molecular surface; they showed, for a group of hydrocarbons, that this contour encompasses more than 97% of the total electronic charge.

### *Electrostatic Potential*

The electrostatic potential  $V(\mathbf{r})$  that is created in the space around a molecule by its nuclei and electrons is given by eq. (1),

$$V(\mathbf{r}) = \sum_A \frac{Z_A}{|\mathbf{R}_A - \mathbf{r}|} - \int \frac{\rho(\mathbf{r}') d\mathbf{r}'}{|\mathbf{r}' - \mathbf{r}|} \quad (1)$$

in which  $Z_A$  is the charge on nucleus A, located at  $\mathbf{R}_A$ .  $V(\mathbf{r})$  has long been used as a qualitative guide to molecular reactivity [3,8,27-31]; its most negative values  $V_{\min}$  were taken to indicate sites vulnerable to electrophilic attack, while the overall patterns of positive and negative potentials were analyzed to identify features that promote or inhibit molecular recognition interactions, such as those between drugs and receptors.

While these applications did provide a great deal of useful insight, they were utilizing only a very limited portion of the information available in the electrostatic potential of a molecule. The desirability of extracting more of it was evident. For

example, in a study of solubilities in supercritical CO<sub>2</sub> [32,33], we recognized that these diminished as the potentials on the molecular surfaces of the solutes became more variable. It seemed that a quantitative correlation could be achieved if we had some measure of this variability. After testing several possibilities, we found that the statistical variance of the surface potential,  $\sigma_{\text{tot}}^2$  (defined below), is effective for this purpose. We have similarly introduced other statistically-defined quantities intended to more completely characterize the surface potential  $V_S(\mathbf{r})$ , since this is what appears to be of primary importance in relation to noncovalent interactions. This has been an evolutionary process, the quantities being introduced as the need for them was perceived in seeking to represent a particular macroscopic property. They now include:

- (a)  $\bar{V}_S^+$ ,  $\bar{V}_S^-$  and  $\bar{V}_S$  are the positive, negative and overall average potentials on the surface.

$$\bar{V}_S^+ = \frac{1}{n} \sum_{i=1}^n V_S^+(\mathbf{r}_i) \quad (2)$$

$$\bar{V}_S^- = \frac{1}{m} \sum_{i=1}^m V_S^-(\mathbf{r}_i) \quad (3)$$

$$\bar{V}_S = \frac{1}{m+n} \left[ \sum_{i=1}^n V_S^+(\mathbf{r}_i) + \sum_{i=1}^m V_S^-(\mathbf{r}_i) \right] \quad (4)$$

- (b)  $\Pi$  is the average deviation of  $V_S(\mathbf{r})$ ,

$$\Pi = \frac{1}{m+n} \sum_{i=1}^{m+n} |V_S(\mathbf{r}_i) - \bar{V}_S| \quad (5)$$

which we interpret as a measure of the local polarity that is present even in molecules with zero dipole moment.

(c)  $\sigma_+^2$ ,  $\sigma_-^2$  and  $\sigma_{\text{tot}}^2$  are the positive, negative and total variances of  $V_S(\mathbf{r})$ , which reflect the range or variability of  $V_S(\mathbf{r})$ .

$$\sigma_+^2 = \frac{1}{n} \sum_{i=1}^n \left[ V_S^+(\mathbf{r}_i) - \bar{V}_S^+ \right]^2 \quad (6)$$

$$\sigma_-^2 = \frac{1}{m} \sum_{i=1}^m \left[ V_S^-(\mathbf{r}_i) - \bar{V}_S^- \right]^2 \quad (7)$$

$$\sigma_{\text{tot}}^2 = \sigma_+^2 + \sigma_-^2 \quad (8)$$

$\sigma_+^2$ ,  $\sigma_-^2$  and  $\sigma_{\text{tot}}^2$  emphasize the extrema of  $V_S(\mathbf{r})$ , due to the terms being squared.

Thus,  $\sigma_{\text{tot}}^2$  covers a much greater range of values than does  $\Pi$ . Indeed, despite what may appear to be an element of similarity between them, the two do not necessarily even show the same qualitative trend. For a collection of 100 molecules of various types, the correlation coefficient between  $\sigma_{\text{tot}}^2$  and  $\Pi$  was only 0.677 [34].

(d)  $v$  indicates the degree of balance between the positive and negative surface potentials, whether these be weak or strong.

$$v = \frac{\sigma_+^2 \sigma_-^2}{(\sigma_{\text{tot}}^2)^2} \quad (9)$$

When  $\sigma_+^2 = \sigma_-^2$ , then  $v$  achieves its maximum possible value of 0.25.

The quantities defined above are *global* in nature, in that they explicitly reflect the magnitude of  $V_S(\mathbf{r})$  at each point. We augment them with the total surface area,  $A_S$ , and the portions of it having positive and negative potentials,  $A_S^+$  and  $A_S^-$ . Finally, we also use three *site-specific* quantities:  $V_{\min}$ , which is the overall most negative value of  $V(\mathbf{r})$  in the total three-dimensional space of the molecule, and the positive and negative extrema of the surface potential  $V_S(\mathbf{r})$ ,  $V_{S,\max}$  and  $V_{S,\min}$ .

### *General Interaction Properties Function*

We have shown that subsets of these fourteen global and site-specific quantities can be used to develop analytical expressions for a variety of condensed-phase macroscopic properties that reflect non-covalent interactions [7-10]; many of these were enumerated earlier. Our procedure is to find the optimum fit of an experimental database for the property to a small group (typically three) of the computed quantities for the corresponding molecules. We use as few variables as is consistent with a good representation, in order to not obscure the key physical factors involved in the interactions. We also try to be as general as possible, not restricting the database to any particular chemical category (e.g. hydrocarbons, aromatics, etc.), although this would undoubtedly improve the correlations.

The unified approach that has been described can be summarized conceptually in terms of a General Interaction Properties Function (GIPF), eq. (10):

Property=

$$f[A_S, A_S^+, A_S^-, \bar{V}_S^+, \bar{V}_S^-, \bar{V}_S, \Pi, \sigma_+^2, \sigma_-^2, \sigma_{\text{tot}}^2, v, V_{\text{min}}, V_{S,\text{min}}, V_{S,\text{max}}] \quad (10)$$

All of the variables in eq. (10) are determined computationally; thus it can be used to predict the property for compounds that are not yet known, or are unavailable in amounts sufficient for experimental measurements. Particularly noteworthy is the fact that solid, liquid and solution properties can be expressed in terms of quantities evaluated for an isolated molecule, with no explicit consideration of the effects of the surroundings.

### Some Results

Extensive tabulations of computed values of the quantities in eq. (10), for a variety of molecules, have been published on several occasions [7,34,35] and have been discussed in detail [9,10,34]. In Table 1 are described, for illustrative purposes, a number of the relationships that have been developed. Some interesting features of these will be pointed out.

The first eight properties listed in Table 1 are for pure liquids or solids, and therefore depend upon interactions between molecules of the same kind. We have found that the product  $v\sigma_{\text{tot}}^2$  is often useful in representing such properties. The interactions can be strongly attractive only if *both* the positive and negative molecular surface



potentials reach relatively large magnitudes. Thus not only should  $\sigma_{\text{tot}}^2$  have a high value, but also  $v$  should be near its maximum of 0.250, indicating a high degree of balance. The product  $v \sigma_{\text{tot}}^2$  is a measure of the degree to which these conditions are satisfied.

Properties that involve a second component may be primarily influenced by only the positive or only the negative potentials, depending upon the specific interactions involved. For example, the octanol/water partition coefficient requires  $\sigma_-^2$  but not  $\sigma_+^2$  in its representation. This reflects the importance of the solute's hydrogen bond accepting capacity, as was noted earlier by Kamlet *et al* [43] and by Famini *et al* [44]. Diffusion through gelatin (a mixture of water-soluble proteins) is also promoted by negative potentials and is actually inhibited by positive ones, as seen from the minus sign in front of  $\sigma_+^2$  in Table 1. This is because the nitrogen and oxygen lone pairs of the protein amide groups attract positive regions on the diffusing molecules, thereby hindering them, but repel negative regions.

There are interesting contrasts between the expressions for free energy of solvation in nonpolar solvents and in water. In the former, stabilization depends upon total surface area and the global quantity  $\Pi$ , the average deviation of  $V_S(\mathbf{r})$ . The destabilizing contribution from  $A_S^+ \bar{V}_S^+$  presumably reflects repulsion between positive regions on the solute and the hydrogens of the hydrocarbon solvent. In water, however, the site-specific quantities  $V_{\text{min}}$ ,  $V_{S,\text{max}}$  and  $V_{S,\text{min}}$  have important roles in enhancing stabilization, due to the importance of hydrogen bonding.

Some of the terms in GIPF relationships, such as those in Table 1, may be contrary to intuitive expectations, or may seem to counter the effects of others. An example is in the expression for  $\Delta G_{\text{solv}}$  in water, in which two terms are reciprocals of one another. However numerical analysis of their quantitative contributions to the property in question, taking into account their coefficients in the equation, usually shows that one of them has the function of correcting or moderating excesses of the other.

Two important points that should be addressed are the extents to which GIPF relationships depend upon (a) molecular conformation, and (b) the computational level. These issues have been investigated, and it appears that they are usually of little practical significance. The computed surface quantities are generally little affected by conformational changes, unless these considerably diminish internal polarity [45], for example by resulting in an intramolecular interaction such as hydrogen bonding. Furthermore, the trends in these quantities were found to be quite similar by different computational procedures [46], so that the statistical characterization of the surface potential should be qualitatively reasonably independent of this factor as should the functional forms of GIPF relationships (although not the numerical coefficients).

## Some Other Applications

### *Heats of Formation of Liquids and Molecular Solids*

Using *ab initio* or density functional techniques, the gas phase heats of formation of compounds of practical significance can now be computed at a rather high level of accuracy [47-56], for example by calculating  $\Delta H$  for the formation of the molecule from its elements, by means of appropriate isodesmic or homodesmic reactions, by using atom or group equivalents, etc. In practice, however, it is often the liquid or solid phase heat of formation that is needed. These can readily be obtained from the gas phase value, provided that the heats of vaporization and sublimation are available:

$$\Delta H_f(\text{liquid}) = \Delta H_f(\text{gas}) - \Delta H_{\text{vap}} \quad (11)$$

$$\Delta H_f(\text{molecular solid}) = \Delta H_f(\text{gas}) - \Delta H_{\text{sub}} \quad (12)$$

$\Delta H_{\text{vap}}$  and  $\Delta H_{\text{sub}}$  can now be determined from the molecular surface electrostatic potential (Table 1). Thus one of the important applications of the GIPF approach is in calculating the heats of formation of liquids and molecular solids [37,55-57].

### *Heats of Formation of Ionic Solids*

For a solid that is ionic rather than molecular, the procedure is somewhat different [42,56], involving its lattice enthalpy,  $\Delta H_{\text{lattice}}$ :

$$\Delta H_f(\text{ionic solid}) = \Delta H_f(\text{positive ion, gas}) + \Delta H_f(\text{negative ion, gas}) - \Delta H_{\text{lattice}}(\text{ionic solid}) \quad (13)$$

The lattice enthalpy is readily derived from the lattice energy [58], for which GIPF expressions have also been developed (Table 1).

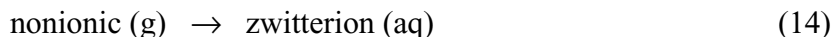
### *Molecular Design and Evaluation*

It is sometimes desired to identify or perhaps design a molecule with a specific type of interactive behavior. An effective means of doing this can be through the characterization of the molecular surface electrostatic potential in terms of the statistical quantities that have been discussed. This can be done prior to attempting the synthesis of the compound, and may suggest structural changes that would enhance the properties being sought. In one study, we evaluated several proposed simulants of toxic chemical defense agents by comparing their  $\Pi$ ,  $\sigma_+^2$ ,  $\sigma_-^2$ ,  $\sigma_{\text{tot}}^2$ ,  $v$  and surface areas to those of the molecules that they are to mimic, to ascertain which ones show the greatest similarity [10,59]. In the context of hapten design, we examined a group of eight mono- and disubstituted benzene derivatives [60]; a close match was found only between chloro- and bromobenzene, but not fluorobenzene.

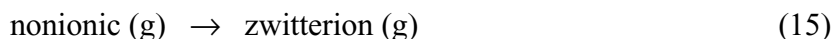
Surface potentials can also provide insight into the feature or features of a group of molecules that are responsible for some specific reactive behavior that they have in common. Thus, a study of 21 anticonvulsants of various chemical types showed all of them to have (a) relatively high  $\sigma_-^2$ , suggesting that their interactions with receptors involve positive regions on the latter, and (b) intermediate  $\Pi$  values, within a rather narrow range which may reflect an optimum balance between hydrophilicity and hydrophobicity [61].

## *Free Energies of Solvation of Zwitterions*

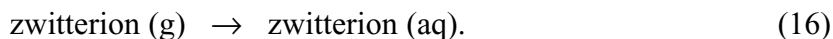
Certain molecules, including many naturally-occurring amino acids, exist in nonionic forms in the gas phase but are converted to tautomeric zwitterions in aqueous solution [62]. We have shown [46] that the free energy change associated with the process,



can be obtained to good accuracy by calculating  $\Delta G$  for the gas phase reaction,



and combining it with the GIPF aqueous solvation free energy of the zwitterion (Table 1), i.e.,  $\Delta G$  for,



## **Summary**

The GIPF approach is a unified computational procedure for representing, predicting and analyzing condensed-phase macroscopic properties that depend upon noncovalent interactions. It is based upon the detailed statistical characterization of the electrostatic potentials on the surfaces of gas phase molecules. The relationships that are obtained serve not only in a predictive capacity, but as well to provide insight into the factors governing the interactions. The statistical analysis of surface potentials is also an effective tool for designing and evaluating molecules with specific types of interactive behavior.

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## References

- [1] J. O. Hirschfelder, C. F. Curtiss and R. B. Bird, *Molecular Theory of Gases and Liquids*, Wiley, New York, 1954, pp. 916-1049.
- [2] J. O. Hirschfelder, in *Molecular Forces*, North-Holland, Amsterdam, 1967, sect. 4, pp. 1-61.
- [3] G. Naray-Szabo and G. G. Ferenczy, *Chem. Rev.*, 95 (1995) 829-847.
- [4] R. P. Feynman, *Phys. Rev.*, 56 (1939) 340-343.
- [5] K. L. C. Hunt, *J. Chem. Phys.*, 92 (1990) 1180-1187.
- [6] A. D. Buckingham, in *Molecular Forces*, North-Holland, Amsterdam, 1967, sect. 2, pp. 1-16.
- [7] J. S. Murray and P. Politzer, in P. Politzer and J. S. Murray (Eds.), *Quantitative Treatments of Solute/Solvent Interactions*, Elsevier, Amsterdam, 1994, pp. 243-289.
- [8] J. S. Murray and P. Politzer, in P. von R. Schleyer (Ed.), *Encyclopedia of Computational Chemistry*, vol. 2, Wiley, New York, 1998, pp. 912-920.
- [9] J. S. Murray and P. Politzer, *J. Mol. Struct. (Theochem)*, 425 (1998) 107-114.
- [10] P. Politzer and J. S. Murray, *Trends Chem. Phys.*, in press.
- [11] M. J. Kamlet, R. M. Doherty, J.-L. M. Abboud, M. H. Abraham and R. W. Taft, *Chemtech*, 16 (1986) 566-576.
- [12] M. J. Kamlet, R. M. Doherty, G. R. Famini and R. W. Taft, *Acta Chem. Scand. B*, 41 (1987) 589-598.
- [13] C. J. Cramer, G. R. Famini and A. H. Lowrey, *Acc. Chem. Res.*, 26 (1993) 599-605.
- [14] A. J. Leo, *Chem. Rev.*, 93 (1993) 1281-1306.
- [15] P. Politzer and J. S. Murray (Eds.), *Quantitative Treatments of Solute/Solvent Interactions*, Elsevier, Amsterdam, 1994.
- [16] M. Karelson, V. S. Lobanov and A. R. Katritzky, *Chem. Rev.*, 96 (1996)

1027-1043.

- [17] J. S. Murray, P. Politzer and G. R. Famini, *J. Mol. Struct. (Theochem)*, 454 (1998) 299-306.
- [18] G. R. Famini and L. Y. Wilson, *J. Phys. Org. Chem.*, 12 (1999) 645-653.
- [19] F. M. Richards, *Annu. Rev. Biophys. Bioeng.*, 6 (1977) 151-176.
- [20] P. K. Weiner, R. Langridge, J. M. Blaney, R. Schaefer and P. A. Kollman, *Proc. Nat. Acad. Sci.*, 79 (1982) 3754-3758.
- [21] M. L. Connolly, *Science*, 221 (1983) 709-713.
- [22] P. A. Bash, N. Pattabiraman, C. Huang, T. E. Ferrin and R. Langridge, *Science*, 222 (1983) 1325-1327.
- [23] M. M. Francl, R. F. Hout, Jr. and W. J. Hehre, *J. Am. Chem. Soc.*, 106 (1984) 563-570.
- [24] J. P. Ritchie, *J. Am. Chem. Soc.*, 107 (1985) 1829-1837.
- [25] R. F. W. Bader, M. T. Carroll, J. R. Cheeseman and C. Chang, *J. Am. Chem. Soc.*, 109 (1987) 7968-7979.
- [26] J. Brickmann, T. Exner, M. Keil, R. Marhofer and G. Moeckel, in P. von R. Schleyer (Ed.), *Encyclopedia of Computational Chemistry*, vol. 3, Wiley, New York, 1998, pp. 1678-1693.
- [27] E. Scrocco and J. Tomasi, *Topics Curr. Chem.*, 42 (1973) 95-170.
- [28] P. Politzer and K. C. Daiker, in B. M. Deb (Ed.), *The Force Concept in Chemistry*, Van Nostrand Reinhold, New York, 1981, pp. 294-387.
- [29] P. Politzer and D. G. Truhlar (Eds.), *Chemical Applications of Atomic and Molecular Electrostatic Potentials*, Plenum, New York, 1981.
- [30] P. Politzer, P. R. Laurence and K. Jayasuriya, *Env. Health Persp.*, 61 (1985) 191-202.
- [31] P. Politzer and J. S. Murray, in K. B. Lipkowitz and D. B. Boyd (Eds.), *Reviews in Computational Chemistry*, vol. 2, VCH, New York, 1991, pp. 273-312.

- [32] P. Politzer, P. Lane, J. S. Murray and T. Brinck, *J. Phys. Chem.*, 96 (1992) 7938-7943.
- [33] P. Politzer, J. S. Murray, P. Lane and T. Brinck, *J. Phys. Chem.*, 97 (1993) 729-732.
- [34] J. S. Murray, T. Brinck, P. Lane, K. Paulsen and P. Politzer, *J. Mol. Struct. (Theochem)*, 307 (1994) 55-64.
- [35] T. Brinck, J. S. Murray and P. Politzer, *J. Org. Chem.*, 58 (1993) 7070-7073.
- [36] J. S. Murray, P. Lane, T. Brinck, K. Paulsen, M. E. Grice and P. Politzer, *J. Phys. Chem.*, 97 (1993) 9369-9373.
- [37] P. Politzer, J. S. Murray, M. E. Grice, M. DeSalvo and E. Miller, *Mol. Phys.*, 91 (1997) 923-928.
- [38] J. S. Murray, T. Brinck and P. Politzer, *Chem. Phys.*, 204 (1996) 289-299.
- [39] J. S. Murray, F. Abu-Awwad and P. Politzer, *J. Phys. Chem. A*, 103 (1999) 1853-1856.
- [40] P. Politzer, J. S. Murray and F. Abu-Awwad, *Int. J. Quantum Chem.*, 76 (2000) 643-647.
- [41] P. Politzer, J. S. Murray and P. Flodmark, *J. Phys. Chem.*, 100 (1996) 5538-5540.
- [42] P. Politzer and J. S. Murray, *J. Phys. Chem. A*, 102 (1998) 1018-1020.
- [43] M. J. Kamlet, R. M. Doherty, M. H. Abraham, Y. Marcus and R. W. Taft, *J. Phys. Chem.*, 92 (1988) 5244-5255.
- [44] G. R. Famini, C. A. Penski and L. Y. Wilson, *J. Phys. Org. Chem.*, 5 (1992) 395-408.
- [45] J. S. Murray, Z. Peralta-Inga and P. Politzer, *Int. J. Quantum Chem.*, 75 (1999) 267-273.
- [46] J. S. Murray, Z. Peralta-Inga and P. Politzer, *Int. J. Quantum Chem.*, submitted.
- [47] D. Habibollahzadeh, M. E. Grice, M. C. Concha, J. S. Murray and P. Politzer, *J. Comp. Chem.*, 16 (1995) 654-658.
- [48] S. J. Mole, X. Zhou and R. Liu, *J. Phys. Chem.*, 100 (1996) 14665-14671.



- [49] A. Nicholaides, A. Rauk, M. N. Glukhovtsev and L. Radom, *J. Phys. Chem.*, 100 (1996) 17460-17464.
- [50] J. Cioslowski, G. Liu and P. Piskorz, *J. Phys. Chem. A*, 102 (1998) 9890-9900.
- [51] S. A. Kafafi and E.-S. R. H. El-Gharkawy, *J. Phys. Chem. A*, 102 (1998) 3202-3208.
- [52] L. A. Curtiss, K. Raghavachari, P. C. Redfern and B. B. Stefanov, *J. Chem. Phys.*, 108 (1998) 692-697.
- [53] G. A. Petersson, D. K. Malick, W. G. Wilson, J. W. Ochterski, J. A. Montgomery, Jr. and M. J. Frisch, *J. Chem. Phys.*, 109 (1998) 10570-10579.
- [54] P. Politzer, P. Lane and M. C. Concha, *J. Phys. Chem. A*, 103 (1999) 1419-1425.
- [55] B. M. Rice, S. V. Pai and J. Hare, *Combust. Flame*, 118 (1999) 445-458.
- [56] P. Politzer, M. E. Grice and J. S. Murray, *Recent Res. Dev. Phys. Chem.*, 3 (1999) 95-109.
- [57] P. Politzer, J. S. Murray and M. E. Grice, *Mat. Res. Soc. Symp. Proc.*, 418 (1996) 55-66.
- [58] D. R. Lide (Ed.), *Handbook of Chemistry and Physics*, 78th ed., CRC Press, New York, 1997.
- [59] P. Politzer, J. S. Murray, M. C. Concha and T. Brinck, *J. Mol. Struct. (Theochem)*, 281 (1993) 107-111.
- [60] P. Politzer, J. S. Murray, T. Brinck and P. Lane, in J. O. Nelson, A. E. Karu and R. B. Wong (Eds.), *Immunoanalysis of Agrochemicals: Emerging Technologies*, ACS Symp. Ser. 586, American Chemical Society, Washington, DC, 1995, pp. 109-118.
- [61] J. S. Murray, F. Abu-Awwad, P. Politzer, L. C. Wilson, A. S. Troupin and R. E. Wall, *Int. J. Quantum Chem.*, 70 (1998) 1137-1143.
- [62] M. Jones, Jr., *Organic Chemistry*, 2nd ed., Norton, New York, 2000.

Table 1. Some GIPF relationships.

Property	Nature of relationship	Correlation coefficient	Reference
boiling point	$f[A_S, (v \sigma_{\text{tot}}^2)^{0.5}]$	0.949	36
critical temperature	$f[A_S^{0.5}, (v \sigma_{\text{tot}}^2)^{0.25}]$	0.914	36
heat of vaporization	$f[A_S^{0.5}, (v \sigma_{\text{tot}}^2)^{0.5}]$	0.965	7
heat of sublimation	$f[A_S^2, (v \sigma_{\text{tot}}^2)^{0.5}]$	0.950	37
heat of fusion	$f[A_S, v\Pi]$	0.919	38
surface tension	$f[A_S^{0.25}, \Pi^2 / A_S, (v \sigma_{\text{tot}}^2)^{1.5}]$	0.923	38
liquid density <sup>a</sup>	$f[M/A_S, \Pi]$	0.982	38
crystal density <sup>a</sup>	$f[M/A_S, \sigma_{\text{tot}}^2 / A_S]$	0.987	38
free energy of solvation in water	$f[V_{\text{min}}, -(V_{S,\text{max}} - V_{S,\text{min}})^3, A_S^- \bar{V}_S^-, (A_S^- \bar{V}_S^-)^{-1}]$	0.988	39
free energies of solvation in benzene, cyclohexane and hexadecane	$f[-A_S^{0.5}, -A_S\Pi, A_S^+ \bar{V}_S^+]$	0.943	40
diffusion constant in gelatin	$f[A_S^{-1}, -\sigma_+^2, \sigma_-^2]$	0.990	41
octanol/water partition coefficient	$f[A_S, -\sigma_-^2, -A_S\Pi]$	0.961	35
lattice energies of Na <sup>+</sup> , K <sup>+</sup> and NH <sub>4</sub> <sup>+</sup> salts <sup>b</sup>	$f[-Q, -V_{S,\text{min}}, -(A_S^- \bar{V}_S^-)^2]$	0.998	42

<sup>a</sup>M is the molecular mass.<sup>b</sup> $V_{S,\text{min}}$ ,  $A_S^-$  and  $\bar{V}_S^-$  are computed for the anion; Q is its charge.